CLAIMS

1. A method of screening for a modulator of Mre11 comprising:
   (a) contacting candidate modulators with Mre11 *in vitro* in the presence of a nucleic acid substrate for Mre11; and
   (b) measuring the hydrolysis of said substrate, whereby a modulator is identified by altering hydrolysis of said substrate compared to a control.

2. The method of claim 1 wherein said nucleic acid substrate is an oligonucleotide with at least 50% nucleotide sequence identity with $(TTAGGG)_n$, wherein n=1 to 20.

3. The method of claim 1 wherein hydrolysis of said nucleic acid substrate is measured by UV absorbance or release of a radiolabel.

4. A method of screening for an agent that specifically binds to Mre11 comprising:
   (a) contacting candidate agents with Mre11; and
   (b) determining whether a candidate agent specifically binds to Mre11.

5. The method of claim 4 wherein Mre11 is attached to a solid support.

6. A method of screening for a modulator of Mre11 comprising:
   (a) providing a cell that expresses Mre11;
   (b) contacting candidate modulators with said cell under conditions in which the modulator is taken up by the cell; and
   (c) measuring a property of said cells selected from the group consisting of cellular proliferation, cellular viability, cellular morphology, SA-β-Gal activity and phosphorylation of p53 or p95, whereby a modulator is identified by altering said property compared to a control.

7. The method of claim 6 wherein said candidate modulators specifically bind to Mre11.

8. The method of any of claims 1-7 wherein said Mre11 is a fragment, homolog, analog or variant of Mre11.

9. The method of claim 8 wherein said fragment, homolog, analog or variant of Mre11 has exonuclease activity.

10. The method of claim 6 wherein the property of said cell is cellular proliferation.

11. The method of claim 6 wherein the property of said cell is cellular viability.

12. The method of claim 6 wherein the property of said cell is cellular morphology.

13. The method of claim 6 wherein the property of said cell is SA-β-Gal activity.

14. The method of claim 6 wherein the property of said cell is phosphorylation of p53 or p95.

15. The method of any of claims 6-7 and 9-14 wherein said cell is a cancer cell.

16. The method of claim 15 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

17. The method of claim 8 wherein said cell is a cancer cell.

18. The method of claim 17 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

19. The method of claim 15 wherein said candidate modulators are selected from the group consisting of carbohydrates, monosaccharides, oligosaccharides, polysaccharides, amino acids, peptides, oligopeptides, polypeptides, proteins, nucleosides, nucleotides, oligonucleotides, polynucleotides, lipids, retinoids, steroids, glycopeptides, glycoproteins, proteoglycans, and small organic molecules.

20. The method of claim 19 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

21. The method of claim 17 wherein said candidate modulators are selected from the group consisting of carbohydrates, monosaccharides, oligosaccharides, polysaccharides, amino acids, peptides, oligopeptides, polypeptides, proteins, nucleosides, nucleotides, oligonucleotides, polynucleotides, lipids, retinoids, steroids, glycopeptides, glycoproteins, proteoglycans, and small organic molecules.

22. The method of claim 21 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

23. A method of screening for modulator of tankyrase comprising:

(a) contacting candidate modulators with tankyrase *in vitro* in the presence of a substrate for tankyrase; and

(b) measuring the ribosylation of said substrate, whereby a modulator is identified by altering ribosylation of said substrate compared to a control.

24. The method of claim 23 wherein said substrate is a peptide or polypeptide.

25. The method of claim 24 wherein said substrate is TRF1.

26. The method of claim 23 wherein ribosylation of said substrate is measured by UV absorbance or labeling of said substrate.

27. A method of screening for an agent that specifically binds to tankyrase comprising:

(a) contacting candidate binders with tankyrase; and

(b) determining whether a candidate agent specifically binds to tankyrase.

28. The method of claim 27 wherein tankyrase is attached to a solid support.

29. A method of screening for modulator of tankyrase comprising:

(a) providing a cell that expresses tankyrase;

(b) contacting candidate modulators with said cell under conditions in which the modulator is taken up by the cell; and

(c) measuring a property of said cells selected from the group consisting of cellular proliferation, cellular viability, cellular morphology, SA-β-Gal activity and phosphorylation of p53 or p95, whereby a modulator is identified by altering said property compared to a control.

30. The methods of claim 29 wherein said candidate modulators specifically bind to tankyrase.

31. The method of any of claims 23-30 wherein said tankyrase is a fragment, homolog, analog or variant of tankyrase that has ribosylation activity.

32. The method of claim 31 wherein said fragment, homolog, analog or variant of tankyrase has ribosylase activity.

33. The method of claim 29 wherein the property of said cell is cellular proliferation.

34. The method of claim 29 wherein the property of said cell is cellular viability.

35. The method of claim 29 wherein the property of said cell is cellular morphology.

36. The method of claim 29 wherein the property of said cell is SA-β-Gal activity.

37. The method of claim 29 wherein the property of said cell is phosphorylation of p53 or p95.

38. The method of any of claims 29-30 and 32-37 wherein said cell is a cancer cell.

39. The method of claim 38 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

40. The method of claim 31 wherein said cell is a cancer cell.

41. The method of claim 40 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

42. The method of claim 38 wherein said candidate modulators are selected from the group consisting of carbohydrates, monosaccharides, oligosaccharides, polysaccharides, amino acids, peptides, oligopeptides, polypeptides, proteins, nucleosides, nucleotides, oligonucleotides, polynucleotides, lipids, retinoids, steroids, glycopeptides, glycoproteins, proteoglycans, and small organic molecules.

43. The method of claim 42 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

44. The method of claim 40 wherein said candidate modulators are selected from the group consisting of carbohydrates, monosaccharides, oligosaccharides, polysaccharides, amino acids, peptides, oligopeptides, polypeptides, proteins, nucleosides, nucleotides, oligonucleotides, polynucleotides, lipids, retinoids, steroids, glycopeptides, glycoproteins, proteoglycans, and small organic molecules.

45. The method of claim 44 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

46. A method of screening for a modulator of MRN complex formation comprising:

(a) contacting candidate modulators with Mre11, Rad50 and Nbs1 *in vitro*; and

(b) measuring the formation of the MRN complex, whereby a modulator is identified by altering formation of the MRN complex compared to a control.

47. The method of claim 46 wherein candidate modulators are contacted with Mre11, Rad50 and Nbs1 in the presence of a nucleic acid substrate or inhibitor of Mre11.

48. The method of claim 47 wherein said nucleic acid is an oligonucleotide with at least 50% nucleotide sequence identity with $(TTAGGG)_n$, wherein n=1 to 20.

49. The method of claim 46 wherein formation of the MRN complex is measured by centrifugation, coprecipitation or nondenaturing electrophoresis.

50. A method of screening for a modulator of the DNA damage pathway comprising:

(a) providing a cell that expresses Mre11 and tankyrase;

(b) contacting candidate modulators with said cell in the presence of an oligonucleotide under conditions in which the modulator is taken up by the cell; and

(c) measuring a property of said cells selected from the group consisting of cellular proliferation, cellular viability, cellular morphology, SA-β-Gal activity and phosphorylation of p53 or p95, whereby a modulator is identified by altering said property compared to a control,

wherein said oligonucleotide has at least 50% nucleotide sequence identity with $(TTAGGG)_n$, wherein n=1 to 20.

51. The method of claim 50 wherein said Mre11 is a fragment, homolog, analog or variant of Mre11.

52. The method of claim 51 wherein said fragment, homolog, analog or variant of Mre11 has exonuclease activity.

53. The method of claim 50 wherein said tankyrase is a fragment, homolog, analog or variant of tankyrase.

54. The method of claim 53 wherein said fragment, homolog, analog or variant of tankyrase has ribosylation activity.

55. The method of claim 50 wherein the property of said cell is cellular proliferation.

56. The method of claim 50 wherein the property of said cell is cellular viability.

57. The method of claim 50 wherein the property of said cell is cellular morphology.

58. The method of claim 50 wherein the property of said cell is SA-β-Gal activity.

59. The method of claim 50 wherein the property of said cell is phosphorylation of p53 or p95.

60. The method of any of claims 50-59 wherein said cell is a cancer cell.

61. The method of claim 61 wherein the telomeres of said cell is maintained by telomerase reverse transcriptase or the ALT pathway.

62. The method of claim 50 wherein said candidate modulators are selected from the group consisting of carbohydrates, monosaccharides, oligosaccharides, polysaccharides, amino acids, peptides, oligopeptides, polypeptides, proteins, nucleosides, nucleotides, oligonucleotides, polynucleotides, lipids, retinoids, steroids, glycopeptides, glycoproteins, proteoglycans, and small organic molecules.

63. A method of treating cancer comprising administering to a subject in need of such treatment a composition comprising an activator of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

64. A method of inducing apoptosis comprising administering to a subject in need of such treatment a composition comprising an activator of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

65. A method of inducing cellular senescence comprising administering to a subject in need of such treatment a composition comprising an activator of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

66. A method of inhibiting tanning comprising administering to a subject in need of such treatment a composition comprising an activator of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

67. A method of promoting cellular differentiation comprising administering to a subject in need of such treatment a composition comprising an activator of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

68. A method of promoting immunosuppression comprising administering to a subject in need of such treatment a composition comprising an activator of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

69. The method of any one of claims 63-68 wherein the activator is an oligonucleotide activator of Mre11 with at least 50% nucleotide sequence identity with $(TTAGGG)_n$ and at least the first x 3'-nucleotide linkages are hydrolyzable by a 3' to 5' nuclease, wherein n=1 to 20, and wherein x is from about 1 to about 10.

70. A method of inhibiting apoptosis comprising administering to a subject in need of such treatment a composition comprising an inhibitor of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

71. A method of inhibiting cellular senescence comprising administering to a subject in need of such treatment a composition comprising an inhibitor of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

72. A method of promoting growth comprising administering to a subject in need of such treatment a composition comprising an inhibitor of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

73. A method of promoting tanning comprising administering to a subject in need of such treatment a composition comprising an inhibitor of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

74. A method of inhibiting cellular differentiation comprising administering to a subject in need of such treatment a composition comprising an inhibitor of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

75. A method of reducing cancer treatment side effects comprising administering to a subject in need of such treatment a composition comprising an inhibitor of Mre11, tankyrase, the DNA damage pathway or MRN complex formation.

76. The method of claim 75 wherein the composition is given in combination with chemotherapy or ionizing radiation.

77. The method of any one of claims 70-76 wherein the inhibitor is an oligonucleotide inhibitor of Mre11 with at least 50% nucleotide sequence identity with $(TTAGGG)_n$ and at least the first x 3'-nucleotide linkages are hydrolyzable by a 3' to 5' nuclease, wherein n=1 to 20, and wherein x is from about 0 to about 10.

78. A composition comprising an oligonucleotide with at least 50% nucleotide sequence identity with $(TTAGGG)_n$ and at least one nonhydrolyzable internucleotide linkage,wherein at least the first x 3'-nucleotide linkages are hydrolyzable by a 3' to 5' nuclease, wherein n=1 to 20, and wherein x is from about 0 to about 10.

79. The composition of claim 78 wherein the 3' to 5' nuclease is Mre11.

80. The composition of claim 78 wherein the oligonucleotide has at least 50% nucleotide sequence identity with TTAGGG.

81. The composition of claim 80 wherein the oligonucleotide or thereof has the sequence GTTAGGGTTAG.

82. The composition of claim 78 wherein the nonhydrolyzable linkage is a phosphorothioate.

83. The composition of claim 78 wherein the oligonucleotide is a PNA.